Amendments to the Specification

Please amend the specification as indicated below, without prejudice or disclaimer. A clean replacement copy of the specification which includes these amendments is attached.

Please replace the paragraph found at p. 1, lines 19-25 with the following replacement paragraph.

Those of skill in the art have therefore desired a method for purifying PT that does not rely on BF. One such method is described by Bogdan, et al. (Appl. Env. Micro. 69(10): 6272-6279, Oct. 2003) Peptides having the ability to mimic the glycosidic moiety of bovine fetuin by binding to PT were identified using a phage display system. Three peptides (3G5: NGSFSGF (SEQ ID NO: 1); 3G8: NGSFSGC (SEQ ID NO: 2); and, 3G2: DGSFSGF (SEQ ID NO: 3) having the consensus sequence XGSFSGX (X is any amino acid; SEQ ID NO: 4) were identified as having PT-binding capacity. 3G2 was also utilized in an affinity column to purify PT from a partially purified PT preparation.

Please replace the paragraphs found at p. 2, line 14 to p. 3, line 20 with the following replacement paragraphs.

Figure 3. Selected gurmarin variants that should be tested for binding activity towards PT. Conserved sequence motifs are highlighted ~~by colored boxes~~. The variants listed are, from top to bottom, SEQ ID NOS. 81-101.

Figure 4. Sequence analysis of the gurmarin selection round 4 against PT. The amino acid sequence of individual variants is shown in the single letter amino acid code. Constant, flanking regions of the library ~~are indicated by light yellow boxes,~~ and constant regions of the gurmarin scaffold are indicated ~~as green boxes~~. The position of the randomized loops 1 and 2 are indicated. The variants are listed from top to bottom in the following order: SEQ ID NOS. 102 (3), 103, 102 (3), 104-110, 102, and 111-147.

Figure 5. Sequence analysis of the gurmarin selection round 5a against PT (epoxy). The amino acid sequence of individual variants is shown in the single letter amino acid code. Constant, flanking regions of the library ~~are indicated by light yellow boxes,~~ and constant regions of the gurmarin scaffold are indicated ~~as green boxes~~. The position of the

randomized loops 1 and 2 are indicated. The variants are listed from top to bottom in the following order: SEQ ID NOS. 148 (3), 149, 148 (2), 150, 151 (2), 148, 152, 151, 148 (5), 153, 148, 154, 148 (4), 154, 148, 155, 148 (2), 156, 157, 155, 158 (2), 159, 148 (4), 160, 148 (2), 161, 148 (4), 162, 148 (2), and 163-169.

Figure 6. Sequence analysis of the gurmarin selection round 5b against PT (strep). The amino acid sequence of individual variants is shown in the single letter amino acid code. Constant, flanking regions of the library ~~are indicated by light yellow boxes,~~ and constant regions of the gurmarin scaffold are indicated ~~as green boxes~~. The position of the randomized loops 1 and 2 are indicated. The variants are listed from top to bottom in the following order: SEQ ID NOS. 170, 171 (16), 172, 173, 174, 171 (2), 175-181, 182 (2), 183 (2), 184, 185 (2), 186 (2), 187-195, 196 (3), 197, and 198.

Figure 7. Sequence analysis of the gurmarin selection round 6a against PT (strep). The amino acid sequence of individual variants is shown in the single letter amino acid code. Constant, flanking regions of the library ~~are indicated by light yellow boxes,~~ and constant regions of the gurmarin scaffold are indicated ~~as green boxes~~. The position of the randomized loops 1 and 2 are indicated. The variants are listed from top to bottom in the following order: SEQ ID NOS. 199 (15), 200, 199 (19), 201, 199 (6), 202, 203 (2), 204, 205 (2), 206, 207, 203, 208, 209, 203, 210, 211, 204, and 212.

Figure 8. Sequence analysis of the gurmarin selection round 6b against PT (strep). The amino acid sequence of individual variants is shown in the single letter amino acid code. Constant, flanking regions of the library ~~are indicated by light yellow boxes,~~ and constant regions of the gurmarin scaffold are indicated ~~as green boxes~~. The position of the randomized loops 1 and 2 are indicated. The variants are listed from top to bottom in the following order: SEQ ID NOS. 213 (2), 214-217, 213, 218, 219, 213, 220, 213 (2), 221, 213 (16), 222, 213 (7), 223, 224, 213 (2), 225, 213, 226, 213 (4), 227-229, 213 (5), 229, 213, 231-242, 213, 242, 213, 243, 213, and 244-252.

Figure 9. Selected PP26 variants that will be tested for binding activity towards PT. Conserved sequence motifs are highlighted as colored letters. The variants, listed from top to bottom, are SEQ ID NOS. 253-269.

Figure 10. Sequence analysis of the PP26 selection round 4 against PT. The amino acid sequence of individual variants is shown in the single letter amino acid code. Constant,

flanking regions of the library are indicated ~~by light yellow boxes~~. The variants are listed from top to bottom in the following order: 253 (6), 270 (3), 271, 272, 271 (2), 273, 274, 275 (2), and 276-305.

Figure 11. Sequence analysis of the PP26 selection round 5a against PT (epoxy). The amino acid sequence of individual variants is shown in the single letter amino acid code. Constant, flanking regions of the library are indicated by light yellow boxes. Conserved sequence motifs are highlighted ~~in red or yellow respectively~~. The variants are listed from top to bottom in the following order: 306, 307 (4), 308-311, 307 (3), 312-315, 312 (6), 316, 312, 316, 312 (7), 317-320, 415, 320 (3), 321 (2), 322 (2), 323, 324 (3), 325-338, 339 (2), 341, and 342.

Figure 12. Sequence analysis of the PP26 selection round 5b against PT (strep). The amino acid sequence of individual variants is shown in the single letter amino acid code. Constant, flanking regions of the library are indicated ~~by light yellow boxes~~. Conserved sequence motifs are highlighted~~ in red or yellow respectively~~. The variants are listed from top to bottom in the following order: 343 (7), 344-346, 345 (5), 347 (2), 345, 348, 347, 345 (2), 349 (4), 350-354, 355 (2), 356 (2), and 357-367.

Figure 13. Sequence analysis of the PP26 selection round 6a against PT. The amino acid sequence of individual variants is shown in the single letter amino acid code. Constant, flanking regions of the library are indicated ~~by light yellow boxes~~. Conserved sequence motifs are highlighted~~ in red or yellow respectively~~. The variants are listed from top to bottom in the following order: 368 (18), 369, 368 (3), 370 (11), 371, 372, 373 (15), 374, 373 (8), 375 (2), 376 (2), 377, 378 (4), 379, 380 (5), and 381-393.

Figure 14. Sequence analysis of the PP26 selection round 6b against PT. The amino acid sequence of individual variants is shown in the single letter amino acid code. Constant, flanking regions of the library are indicated ~~by light yellow boxes~~. The variants are listed from top to bottom in the following order: 394, 395, 396, 397 (40), 398, 399 (5), 400, 399 (13), 401, 399 (7), 400 (2), 401, 402 (2), 403-414.

Please replace the paragraphs found at p. 4, lines 11-18 with the following replacement paragraph.

Figure 20. Elution of PT from peptide streptavidin sepharose under acidic (50 mM glycine, pH 2.5) or basic (100 mM carbonat boffer, pH 10.5) conditions. Peptide bound PT was displaced from the peptide streptavidin sepharose (20 µl containing ~200 pmol of one peptide) by three consecutive washes with with the indicated elution buffers (40 µl each). Remaining material was subsequently eluted with gel loading buffer. All elutions were analyzed on 12% Bis Tris gels (1x MES running buffer) and visualized by silver staining. 1/40 volume of the flow through after peptide streptavidin sepharose incubation with sample A was analyzed was analyzed on the same gel for each peptide.

Please replace the paragraphs found at p. 8, lines 5-17 with the following replacement paragraphs.

Peptides have been identified that bind PT and are described herein. Certain peptides have been found to bind PT with high affinity. Such preferred PT binding peptides include:

RSSHCRHRNCHTITRGNMRIETPNNIRKDA (pp26-5; SEQ ID NO: 5);
STMNTNRMDIQRLMTNHVKRDSSPGSIDA (pp26-6; SEQ ID NO: 6);
RSNVIPLNEVWYDTGWDRPHRSRLSIDDDA (pp26-9; SEQ ID NO: 7);
RSWRDTRKLHMRHYFPLAIDSYWDHTLRDA (pp26-15; SEQ ID NO: 8);
SGCVKKDELCARWDLVCCEPLECIYTSELYATCG (G-9; SEQ ID NO: 9);
SGCVKKDELCELAVDECCEPLECFQMGHGFKRCG (G-10; SEQ ID NO: 10);
SGCVKKDELCSQSVPMCCEPLECKWFNENYGICGS (G-15; SEQ ID NO: 11); and,
SGCVKKDELCELAIDECCEPLECTKGDLGFRKCG (G-19; SEQ ID NO: 12).
Of these, especially preferred peptides include:
RSNVIPLNEVWYDTGWDRPHRSRLSIDDDA (pp26-9; SEQ ID NO: 7); and,
SGCVKKDELCSQSVPMCCEPLECKWFNENYGICGS (G-15; SEQ ID NO: 11).

Please replace the paragraphs found at p. 10, lines 8-22 with the following replacement paragraph.

PT isolated using the methods described herein may be prepared as pharmaceutical compositions. Preferred pharmaceutical compositions include, for example, PT in a liquid preparations such as a suspensions, syrups, or elixirs. Preferred

injectable preparations include, for example, peptides suitable for parental, subcutaneous, intradermal, intramuscular or intravenous administration such as sterile suspensions or emulsions. For example, PT may be prepared as a composition in admixture with a suitable carrier, diluent, or excipient such as sterile water, physiological saline, glucose or the like. The composition may also be provided in lyophilized form for reconstituting, for instance, in isotonic aqueous, saline buffer. Such compositions may also be prepared and utilized as a vaccine as described in, for example, U.S. Pat. No. 5,877,298 and 6,399,076 (Vose, et al.) as well as International App. No. PCT/CA96/00278. PT prepared as indicated herein may also be combined with other antigens from disease-causing organisms such as Corynbacterium (i.e., diphtheria), Clostridium (i.e., tetanus), polio virus (i.e., IPV, OPV), hepatitis virus, Neisseria (i.e., meningitis), Streptococcus, Hemophilus, or other pertussis antigens (i.e., filamentous hemagglutinin, pertactin, and agglutinogens), among others as is known in the art.

Please replace the paragraphs found at p. 11, lines 2-22 with the following replacement paragraphs.

Gurmarin is a 35-residue polypeptide from the Asclepiad vine *Gymnea sylvestre.* It has been utilized as a pharmacological tool in the study of sweet-taste transduction because of its ability to selectively inhibit the neural response to sweet tastants in rats. It has no apparent effect in humans. It has been suggested that the taste-suppressing of gurmarin might be due to the peptide either by binding directly to a sweet-taste receptor or interacting with a downstream target in the sweet-taste-transduction system ~~(1)~~.

Gurmarin belongs to the family of "knottins", a group of structurally related proteins, typically less than 40 residues in length. Knottins bind to a diverse range of molecular targets that includes proteins, sugars and lipids but share a common scaffold comprising a small triple-stranded antiparallel β-sheet and disulphide bound framework ~~(2,3)~~.

A specialized gurmarin-library was designed with 15 randomized amino acid positions, as shown below:

`Wild-type gumarin: qqCVKKDELCIPYYLDCCEPLECKKVNWWDHKCig (SEQ ID NO: 13)`

Gumarin core: CVKKDELCXXXXXXCCEPLECXXXXXXXXXC (SEQ ID NO: 14)

Within the gumarin core sequence, X represents any amino acid. This library was validated to yield high affinity binders against protein targets. The gurmarin library combines a set of advantages that makes it the best choice for a selection against the PT-toxin for at least the following reasons: limited flexibility makes up for high entropic cost in conforming to target topology; theoretically fewer amino acids for higher affinities than in linear libraries; resistant to proteases; and susceptibility to redox-elution conditions in downstream applications. The gurmarin library was constructed using process shown in **Figure 1**.

Please replace the paragraph found at p. 12, lines 12-18 with the following replacement paragraph.

Three gel-purified oligos were used to construct the gurmarin library with two randomized loops. 1 nmole of gurmarin template (≈ ca. $6 \cdot 10^{14}$ sequences) 5'- AGT GGC TCA AGC TCA GGA TCA GGC TGC GTC AAG AAA GAC GAG CTC TGC NNS NNS NNS NNS NNS NNS TGC TGT GAG CCC CTC GAG TGC NNS NNS NNS NNS NNS NNS NNS NNS NNS TGC GGC AGC GGC AGT TCT GGG TCT AGC-3' (SEQ ID NO: 15), was amplified for 6 rounds of PCR (94°C, 1 min; 65°C, 1 min; 72°C, 1 min) using 1 μM of the 5'-His-Tag Primer 5'-TAA TAC GAC TCA CTA TAG GGA CAA TTA CTA TTT ACA ATT ACA ATG CAC CAT CAC CAT CAC CAT AGT GGC TCA AGC TCA GGA TCA-3' (SEQ ID NO: 16) and 1 μM of the 3'-Primer 5'-TTT TAA ATA GCG GAT GCT ACT AGG CTA GAC CCA GAA CTG CCG CT-3' (SEQ ID NO: 17) using *Taq*-polymerase and analyzed on a 2 % agarose gel, which indicated a representative library had been constructed.

Please replace the paragraph found at p. 13, lines 18-28 with the following replacement paragraph.

A specialized linear peptide library PP26 with 26 randomized amino acid positions was also designed using the following construct:

T7-TMV-MGRGS-HHHHHH-ARS-XXXXXXXXXXXXXXXXXXXXXXXXX-DANAPK-ASAI (SEQ ID NO: 19). The sequence of the protein portion (50 amino acids in length) is shown in the single letter amino acid code, where X represents any amino acid. Portions of the library that are not translated include: (a) T7: the T7-promoter for optimal *in vitro* transcription of library; and, (b) TMV: the *Tabaco Mosaic Virus* translation initiation sequence for perfect *in vitro* translation of library. MGRGS represents a structural, flexible linker. HHHHHH (SEQ ID NO: 20) represents a His_6-tag for efficient affinity purification of PROfusion™ library. ARS represents a second structural, flexible linker. DANAPK (SEQ ID NO: 21) represents a third structural, flexible linker. ASAI represents an optimized linker for efficient coupling with puromycin-acceptor-molecule.

Please replace the paragraph found at p. 14, lines 2-12 with the following replacement paragraph.

Three gel-purified oligos were used to construct the gurmarin library with two randomized loops. 1 nmole of PP26 template (≈ ca. $6 \cdot 10^{14}$ sequences) 5'-AGC GGA TGC CTT CGG AGC GTT AGC GTC SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN SNN AGA TCT AGC ATG ATG ATG ATG A-3' (SEQ ID NO: 22), was amplified for 6 rounds of PCR (94°C, 1 min; 65°C, 1 min; 72°C, 1 min) using 1 μM of the 5'-His-Tag Primer 5'-TAA TAC GAC TCA TAG GGA CAA TTA CTA TTT ACA ATT ACA ATG GGA CGT GGC TCA CAT CAT CAT CAT CAT CAT GCT AGA TCT -3' (SEQ ID NO: 23) and 1 μM of the 3'-Primer 5'-AA TTA AAT AGC GGA TGC CTT CGG AGC GTT AGC -3' (SEQ ID NO: 24) using *Taq*-polymerase and confirmed by analysis on a 2 % agarose gel.

Please replace the paragraph found at p. 14, lines 22-27 with the following replacement paragraph.

Purified RNA will be annealed (85°C, 1 min △ cool down to 25°C at a ramp of 0.3°C/s) to a 1.5-fold excess of puromycin-oligonucleotide linker PEG2A18: 5'-psoralen-*UAG CGG AUG C* A_{18} $(PEG\text{-}9)_2$ CC puromycin (SEQ ID NO: 18; nucleotides shown in italics represent 2'-O-methyl-derivatives). The covalent coupling is performed by

illumination for 15 min at RT (RT) with UV-light (365 nm). The reaction product was analyzed on 6%-TBU gel and indicated the linking reaction had proceeded efficiently.

Please replace the paragraph found at p. 20, lines 18-22 with the following replacement paragraph.

The gurmarin DNA-pools resulting from selection rounds R4, R5 and R6 were cloned into the pCR®2.1-TOPO®-vector using the TOPO TA Cloning® kit (Invitrogen). The gurmarin DNA was ligated to the pCR®2.1-TOPO®-vector in different concentrations. For 6 µl reactions, 0.5 µl, 2 µl and 4 µl of the gurmarin pool DNA were used respectively. The ligation was performed according to the manufacturer's instructions.

Please replace the paragraph found at p. 20, line 33 to p. 21, line 6 with the following replacement paragraph.

From each individual clone, plasmid DNA was prepared and subjected to an automated DNA-sequencing procedure using a M13-primer 5'- TGT AAA ACG ACG GCC AGT-3' (SEQ ID NO: 25). As shown in Figures 3-8, a single gurmarin sequence variant begins to be significantly enriched in selection round 4 and represents > 90 % of all sequences after selection round 6. This clearly indicates that this variant probably binds with the highest affinity to PT. In addition to this most prominent sequence variant, a variety of other gurmarin sequences have been enriched that partially share common sequence motifs. This finding indicates that these other sequences show affinity towards PT as well.

Please replace the paragraph found at p. 22, lines 7-14 with the following replacement paragraph.

From each individual clone plasmid DNA was prepared and subjected to an automated DNA-sequencing procedure using a M13-primer 5'- TGT AAA ACG ACG GCC AGT-3' (SEQ ID NO: 25). As shown in **Figures 9-14**, two main variants have been enriched during the selection rounds. Both variants share a common conserved sequence motif. This finding indicates that the side chains of the conserved amino acids putatively

establish a direct interaction with a certain PT surface region. Furthermore, at least 4 additional variants have been enriched at lesser extent. Since these variants do not comprise the above mentioned conserved sequence motif it can be concluded that these variants potentially bind to different surface regions of PT.

Please replace the paragraph found at p. 23, line 18-31 with the following replacement paragraph.

Purified RNA was annealed (85°C, 1 min cool down to 25°C at a ramp of 0.3°C/s) to a 1.5-fold excess of puromycin-oligonucleotide linker PEG2A18: 5'-psoralen-*UAG CGG AUG C* A_{18} (PEG-9)$_2$ CC puromycin (nucleotides shown in italics represent 2'-O-methyl-derivatives; SEQ ID NO: 17). The covalent coupling was performed by illumination for 15 min at RT (RT) with UV-light (365 nm). The reaction product was analyzed on 6%-TBU gel. Ligated RNA was translated using the rabbit reticulocyte lysate from Promega in the presence of 15 µCi ^{35}S-methionine (1000 Ci/mmole). After a 30 min incubation at 30°C, KCl and $MgCl_2$ were added to a final concentration of 530-mM and 150 mM respectively and a sample was analyzed on 4-20% Tris/glycine-SDS-PAGE. mRNA-protein fusions (PROfusions ™) were isolated by incubation with oligo dT magnetic beads (Miltenyi) in incubation buffer (100 mM Tris-HCl pH 8.0, 10 mM EDTA, 1 mM NaCl and 0.25 % Triton X-100) for 5 min at 4°C. PROfusion™ molecules were isolated by filtration through MiniMACS-columns (Miltenyi), washing with incubation buffer and elution with water. A sample was analyzed on 4-20% Tris/glycine-SDS-PAGE.

Please replace the paragraph found at p. 21, line 24 to p. 22, line 4 with the following replacement paragraph.

The PP26 DNA-pools resulting from selection rounds R4, R5 and R6 were cloned into the pCR®2.1-TOPO®-vector using the TOPO TA Cloning® kit (Invitrogen). The PP26 DNA was ligated to the pCR®2.1-TOPO®-vector in different concentrations. For 6 µl reactions 0,5 µl / 2 µl and 4 µl of the gurmarin pool DNA were used respectively. The ligation was performed according to the manufacturer's instructions. 2 µl of these ligations were transformed into 20 µl of the *E. coli* Top 10 F' competent cells

(Invitrogen) and spread out on LB plates containing 50 µg/ml Kanamycin and 0,5 % Glucose. From each of these transformations 150 single colonies were picked to a masterplate containing 50 µg/ml Kanamycin and 0,5 % Glucose to repress T7 dependaent protein expression and a second plate containing X-Gal and IPTG for a blue white screening. For each Transformation 96 of the colonies from the repressed masterplate corresponding to the white colonies from the blue white test were used to inoculate a 96 well LB agar plate and 500 µl liquid cultures (LB containing 50 µg/ml Kanamycin and 0,5 % Glucose). The 96 well agar plates were sent out for commercial sequencing service. The liquid cultures were mixed with 500 µl 40 % Glycerol, frozen in liquid nitrogen and stored at – 80 °C.

Please replace Table 3 on pp. 24-25 with the following replacement Table 3.

Table 3
Post selection analysis of gurmarin-variants*

#	seq #	peptide sequence	test 1	test 2	SEQ ID
1	194227	MHHHHHHSGSSSGSGCVKKDELCAGSVGHCCEPLECLRRFLNLRWCGSGSSGSS	-	n.d.	26
2	194238	MHHHHHHSGSSSGSGCVKKDELCIVMRAPCCEPLECLRRYMLKHMCGSGSSGSS	-	n.d.	27
3	194239	MHHHHHHSGSSSGSGCVKKDELCKAFRYSCCEPLECLRKWLKARFCGSGSSGSS	-	n.d.	28
4	194251	MHHHHHHSGSSSGSGCVKKDELCLRSSIDCCEPLECLYKWMQRRLCGSGSSGSS	-	n.d.	29
5	194210	MHHHHHHSGSSSGSGCVKKDELCWPRRHKCCEPLECLLEMLERKRCGSGSSGSS	-	n.d.	30
6	194261	MHHHHHHSGSSSGSGCVKKDELCMSMACVCCEPLECKYHGYFWLCGSGSSGSS	-	n.d.	31
7	194214	MHHHHHHSGSSSGSGCVKKDELCAVWFDVCCEPLECTYQSGYYWLCGSGSSGSS	-	n.d.	32
8	194226	MHHHHHHSGSSSGSGCVKKDELCEPWYWRCCEPLECVYTSGYYYSCGSGSSGSS	-	n.d.	33
9	194259	MHHHHHHSGSSSGSGCVKKDELCARWDLVCCEPLECIYTSELYATCGSGSSGSS	√	√	34
12	194297	MHHHHHHSGSSSGSGCVKKDELCVFYFPNCCEPLECRWVNDNYGWCGSGSSGSS	√	-	35
13	194330	MHHHHHHSGSSSGSGCVKKDELCMSMACVCCEPLECKYHGYFWLCGSGSSGSS	√	-	36
14	194479	MHHHHHHSGSSSGSGCVKKDELCTTASKSCCEPLECKWTNEHFGTCGSGSSGSS	√	-	37
15	194511	MHHHHHHSGSSSGSGCVKKDELCSQSVPMCCEPLECKWFNENYGICGSGSSGSS	√	-	38
16	194533	MHHHHHHSGSSSGSGCVKKDELCARWDLVCCEPLECIYTSELYATCGSGSSGSS	√	-	39
17	194486	MHHHHHHSGSSSGSGCVKKDELCARWDLVCCEPLECLGHGLGYAYCGSGSSGSS	-	n.d.	40
18	194668	MHHHHHHSGSSSGSGCVKKDELCMWSREVCCEPLECYYTGWYWACGSGSSGSS	-	-	41
10	194264	MHHHHHHSGSSSGSGCVKKDELCELAVDECCEPLECFQMGHGFKRCGSGSSGSS	√	√	42
19	194737	MHHHHHHSGSSSGSGCVKKDELCELAVDECCEPLECTKGDLGFRKCGSGSSGSS	√	√	43
20	194716	MHHHHHHSGSSSGSGCVKKDELCELAIDVCCEPLECLGHGLGYAYCGSGSSGSS	√	n.d.	44
21	194720	MHHHHHHSGSSSGSGCVKKDELCELAIDVCCEPLECLGHGLGYAYCGSGSSGSS	-	-	45
11	194328	MHHHHHHSGSSSGSGCVKKDELCNWVTPMRCEPLECLGHGLGYAYCGSGSSGSS	√	n.d.	46

Please replace Table 4 on p. 25 with the following replacement Table 4.

Table 4

Post selection analysis of PP26-variants*

#	seq #	peptide sequence	test 1	test 2	SEQ ID
1	197569	MGRGSHHHHHHARSDWELSPPHVAITTRHLINCTDGPLLRDANAPKASAI	-	n.d.	47
2	197536	MGRGSHHHHHHARSLNGESTSNILTTSRKVTEWTGYTASVDANAPKASAI	-	n.d.	48
3	197611	MGRGSHHHHHHARSQVTWHHLADTVTTKNRKCTDSYIGWNXANAPKASAI	-	n.d.	49
4	197530	MGRGSHHHHHHARSIIVIHNAIQTHTPHQVSIWCPPKHNRDANAPKASAI	-	n.d.	50
5	197557	MGRGSHHHHHHARSSHCRHRNCHTITRGNMRIETPNNIRKDANAPKASAI	√	√	51
6	197596	MGRGSHHHHHHARSTMNTNRMDIQRLMTNHVKRDSSPGSIDANAPKASAI	√	√	52
7	197552	MGRGSHHHHHHARSLSALRRTERTWNTIHQGHHLEWYPPADANAPKASAI	-	n.d.	53
8	197541	MGRGSHHHHHHARSWTSMQGETLWRTDRLATTKTSMSHPPDANAPKASAI	-	n.d.	54
9	197588	MGRGSHHHHHHARSNVIPLNEVWYDTGWDRPHRSRLSIDDDANAPKASAI	√	√	55
10	197635	MGRGSHHHHHHARSCLATRNGFVMNTDRGTYVKRPTVLQDANAPKASAI	√	-	56
11	197797	MGRGSHHHHHHARSWGLSGTQTWKITKLATRLHHPEFETNDANAPKASAI	-	n.d.	57
12	197888	MGRGSHHHHHHARSWRWHNWGLSDTVASHPDASNSLNMMYDANAPKASAN	-	n.d.	58
13	197897	MGRGSHHHHHHLDLWGPPSGSPRTRSTTGTSTTSSPSTPGTLTLRRHPH	-	n.d.	59
14	197825	MGRGSHHHHHHARSWQPEVKMSSLVDTSQTVGAAVETRTTDANAPKASA	√	-	60
15	198000	MGRGSHHHHHHARSWRDTRKLHMRHYFPLAIDSYWDHTLRDANAPKASAI	√	-	61
16	197983	MGRGSHHHHHHARSWTSMQGETLWRTDRLATTKTSMSHPPDANAPKASAI	-	n.d.	62
17	197998	MGRGSHHHHHHHARSPLWYHYNCWDTICLADWLKDRPHGVYDANAPKASA	-	n.d.	63
18	197947	MGRGSHHHHHHARSVGTTIRIAQDTEHYRNVYHKLSQYSRDANAPKASAI	√	-	64
19	197954	MGRGSHHHHHHARSVGTTIRIAQDTEHYRNVYHKLSQYSRDANAPKASAI	-	n.d.	65
20	197971	MGRGSHHHHHHARSNVIPLNEVWYDTGWDRPHRSRLSIDDDANAPKASAI	-	n.d.	66

Please replace Table 5 on p. 26 with the following replacement Table 6.

Table 5

Peptide Synthesis of Pertussis Toxin Binding Peptides*

Selection	Clone	Seq #	Sequence	Purity (%)	Yield (mg)	SEQ ID
pp26	5 c	197557-1	RSSHCRHRNCHTITRGNMRIETPNNIRKDAK	90 - 95	7,7	67
pp26	5 n	197557-2	RSSHCRHRNCHTITRGNMRIETPNNIRKDA	90 - 95	7,6	68
pp26	6 n	197596-1	RSTMNTNRMDIQRLMTNHVKRDSSPGSIDA	90 - 95	6,3	69
pp26	9 n	197588-1	RSNVIPLNEVWYDTGWDRPHRSRLSIDDDA	90 - 95	5,8	70
pp26	15n	198000-1	RSWRDTRKLHMRHYFPLAIDSYWDHTLRDA	90-95	4,8	71
gurmarin	9 c	194259-1	SGCVKKDELCARWDLVCCEPLECIYTSELYATCGK	70	1,0	72
gurmarin	9 n	194259-2	SGCVKKDELCARWDLVCCEPLECIYTSELYATCG	80 - 90	4,0	73
gurmarin	10 n	194264-1	SGCVKKDELCELAVDECCEPLECFQMGHGFKRCG	90 - 95	4,9	74
gumarin	15n	194511-1	SGCVKKDELCSQSVPMCCEPLECKWFNENYGICG S	90-95	6,3	75
gurmarin	19 n	194737-1	SGCVKKDELCELAIDECCEPLECTKGDLGFRKCG	90 - 95	6,7	76

Please replace the paragraphs found at p. 26, line 25 to p. 27, line 15 with the following replacement paragraphs.

As template for PCR served the pCR2.1 vector containing the sequences of the identified pp26 binders to PT. The products obtained in a PCR using the oligonucleotides #467 (5′-CATGCCATGGGACGTGGCTCACATCATC-3′; SEQ ID NO: 77) and #468 (5′-phosphate-GGGTTAAATAGCGGATGCCTTCGGAGCGTTAGCGTC-3′; SEQ ID NO: 78) with *Pwo* DNA polymerase (Roche) were digested with *Nco*I (New England Biolobs). A modified vector (pGEX6P (Amersham/Pharmacia) containing an additional *Nco*I site) was digested with *Nco*I/*Sma*I (New England Biolobs) and the PCR product was directionally cloned into the *Nco*I/*Sma*I site of this vector. After transformation in TOP10 (Invitrogen) positive clones were identified by colony PCR and verified by sequencing.

2. ***Construction of GST fusions for gurmarin-variants***

As template for PCR served the pCR2.1 vector containing the sequences of the identified gurmarin binders to PT. The products obtained in a PCR using the oligonucleotides #464 (5′-GGAGATCTCATATGCACCATCACCATCACCATAGTGGC-3′; SEQ ID NO: 79) and #465 (5′-phosphate- GGGTTAAATAGCGGATGCTACTAGGC-3′; SEQ ID NO: 80) with *Pwo* DNA polymerase (Roche) were digested with *Nde*I (New England Biolobs). A modified vector (pGEX6P (Amersham/Pharmacia) containing an additional *Nde*I site) was digested with *Nde*I/*Sma*I (New England Biolobs) and the PCR product was directionally ligated into the *Nde*/*Sma*I site of this vector. After transformation in TOP10 (Invitrogen) positive clones were identified by colony PCR and verified by sequencing (**Table 6**).

Please replace the paragraph found at p. 34, lines 13-25 with the following replacement paragraph.

As shown above by BIAcore 2000 measurements all PT/peptide complexes were sensitive against 2 M $MgCl_2$, conditions that were shown not to be critical for PT hexamer stability. The elution efficiencies of defined $MgCl_2$ concentrations were evaluated for PT that was bound on streptavidin sepharose via one of the four

immobilized synthetic peptides. 400 pmol of each peptide immobilized on 20 µl sepharose were incubated with 100 µl 50 mM Tris/HCl, pH 7.5 and 100 µl sample A to allow binding of PT. After 4 washes with 50 mM Tris/HCl, pH 7.5 (200 µl each), the bound fraction of PT was eluted using 3 consecutive 20 µl volumes of

(a) 0.2 M $MgCl\cancel{2}_{\underline{2}}$ in 50 mM Tris/HCl, pH 8.5, or

(b) 0.5 M $MgCl\cancel{2}_{\underline{2}}$ in 50 mM Tris/HCl, pH 8.5, or

(c) 1.0 M $MgCl\cancel{2}_{\underline{2}}$ in 50 mM Tris/HCl, pH 8.5, or

(d) 1.5 M $MgCl\cancel{2}_{\underline{2}}$ in 50 mM Tris/HCl, pH 8.5, or

(e) 2.0 M $MgCl\cancel{2}_{\underline{2}}$ in 50 mM Tris/HCl, pH 8.5.

Please replace the paragraphs found at p. 4, line 11-18 with the following replacement paragraphs.

Each column (containing 4 µl sepharose with 400 pmol peptide for pp26/9 and gur/15; 4 µl with undefined amount bound peptide pp26/15; 20 µl with 2000 pmol peptide for gur/9) was incubated with 400 µl Sample B (adjusted to pH 7.0 – 7.5 by addition of HCl) to allow binding of PT. After 5 washes with 50 mM Tris/HCl, pH 7.5 (each 100 µl), PT was eluted from the peptide streptavidin sepharose by consecutive elutions (3 elutions for pp26/9 and gur/15; 4 elutions for pp26/15 and gur/9), as follows:

(a) with 50 mM glycine, pH 2.5 (each 20 µl) in case of column 1, or

(b) with 100 mM carbonate buffer, pH 10.5 (each 20 µl) in case of column 2, or

(c) with 2 M $MgCl_2$ in 50 mM Tris, pH 8.5 (each 20 µl) in case of column 3.

Please delete the term "Confidential" shown with Table 11.

Please replace the Sequence Listing with the new Sequence Listing submitted herewith.